II. Non-technical Abstract

Current therapy of Pediatric HIV infection ultimately does not prevent the relentless destruction of the immune system. Small molecule drug therapies have so far been unable to produce a sufficiently specific inhibition of the virus to allow for complete eradication of the infection. Given the backdrop of an incurable, severe, and chronic disease that is affecting thousands of infants each year, it is reasonable to investigate more risky or speculative therapies. Gene therapy offers several theoretical advantages. Genetic resistance elements are informational molecules that can be designed for high specificity against HIV. HIV resistance genes can be designed to attack complex biological targets and to combine multiple functions. The concept that will be pursued in this project adheres to the long term goal of stably introducing a gene into hematopoietic stem cells. Pediatric AIDS may be particularly amenable to the gene therapy approach since, at least in tissue culture models, the cord blood hematopoietic precursors are more efficiently transduced with retrovirus vectors than are adult marrow cells. We will store cord blood cells from infants at risk of acquiring HIV infection from their mothers. In three babies found to be infected with HIV, we will introduce an HIV resistance gene using a retrovirus vector. Along with this vector we will introduce an inactive control vector that will aid in determining the safety and activity of the anti-HIV vector. The genetically altered cells will be given back to each baby in a manner similar to a blood transfusion. Blood tests will be used to determine whether the anti-HIV vector harms the blood cells expressing it and whether the infants make an immune response to the vector.